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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

PURDY, KYLE A

ART UNIT

PAPER NUMBER

1611

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/561,700	Applicant(s) ODIDI ET AL.	
	Examiner Kyle Purdy	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-48 is/are pending in the application.
- 4a) Of the above claim(s) 29,30 and 46-48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 31-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4 pages (11/07/2008)</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Exhibit A</u> . |

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 11/07/2008 wherein claims 1 and 31 have been amended.
2. Claims 1-28 and 31-45 are presented for examination on the merits. The following rejections are made. Claims 29, 30 and 46-48 stand as withdrawn.

Response to Applicants' Arguments

3. Applicants arguments filed 11/07/2008 regarding the rejection of claims 1-28 and 31-45 made by the Examiner under 35 USC 103(a) over Phillips (US 2002/0045646) in view of Bergstrand et al. (US 5817338) have been fully considered but they are not found persuasive.

4. The rejection of claims 1-28 and 31-45 made by the examiner under 35 USC 103(a) is **MAINTAINED** for the reasons of record in the office action mailed on 03/18/2008.

5. In regards to the 103(a) rejection, Applicant asserts the following:

A) The compositions taught by Philips and Bergstrand do not teach 'distinct' populations for the components of the composition; and

B) Bergstrand teaches away from using a capsule.

6. With respect to assertion A, Applicants arguments are not found persuasive. Claims 1 and 31 have been amended to make them recite the limitation that the components are distinct. But what does such a limitation mean? Distinct according to the definition has a variety of meanings. The definition of 'distinct' is applied according to the definitions set forth by Dictionary.com (Exhibit A). Distinct means, 'not alike', 'dissimilar', or 'separate'. It is the opinion of the Examiner that the composition of Phillips teaches distinct components in all of

Art Unit: 1611

these senses. In the sense that the components are 'not alike', Phillips obviates the instant claims. Each component has distinct properties. For examples, one PPI is released immediately, another PPI is enterically coated and slowly released, and there is a basic substance which is separate from both of the previous actives. Each of these components has a different physical property from the other. Thus, the populations of ingredients in the composition would necessarily be distinct according to this definition. In the sense that the components are 'separate', it is the position of the Examiner that Phillips meets this limitation too. While it may be true that components are admixed together, they still exist as 'separate' entities within the pharmaceutical mixture. Applicant is directed to Example VI of Phillips. Applicants arguments are not found persuasive.

7. With respect to assertion B, the Examiner is perplexed by Applicants argument. Bergstrand is not relied upon for its teaching a capsule structure. The primary reference to Phillips suggests that limitation. Bergstrand is relied upon for their teaching of a separating layer between the PPI core and the enteric coating layer. As was noted in the office action mailed on 03/18/2008, Bergstrand teaches that PPI compounds are acid labile and the enteric coatings are generally acidic. If the PPI core were coated directly with an enteric coating, the PPI would slowly degrade thereby eliminating some of the PPIs pharmaceutical efficacy. Bergstrand teaches that by putting an alkaline separating layer between the core and the enteric coating layer results in a more chemically stable structure suitable for long term storage. One would have been motivated to include in the capsule formulation taught by Phillips such an enterically coated PPI granule comprising a separating layer between the enteric coating and the core. Applicants argument is not found persuasive.

Maintained Rejections
Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-28 and 31-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US 2002/0045646, 04/18/2002; of record, see IDS) and Bergstrand et al. (US 5817338, 10/06/1998; of record, cited in prior office action).

10. Phillips is drawn to a composition for treating gastric disorders employing proton pump inhibitors (PPIs) in a pharmaceutically acceptable carrier. It is taught that the PPI can be any substituted benzimidazole compound possessing H⁺, K⁺-ATPase inhibiting activity and being unstable to acid (i.e. acid labile). The composition of Phillips can be a powder, tablet, capsule and a two part tablet (see [0036]; see instant claims 1 and 31). It is taught that upon oral administration of the PPI the drug may be absorbed into the bloodstream where the compound is eventually delivered to the acid secreting portion of the parietal cells of the stomach. The PPIs included within the teaching of Phillips include omeprazole, lansoprazole and rabeprazole. It is noted by Phillips that such PPIs are readily degraded under acidic conditions such as that of the stomach and a useful way to circumvent degradation is to include at least one buffering agent (i.e. basic substance). Basic substances include sodium bicarbonate, magnesium hydroxide and aluminum hydroxide (see [0054]; see instant claims 21 and 40). Moreover, the basicity of base

Art Unit: 1611

used must be strong enough to elevate the pH of the stomach sufficiently to prevent significant degradation of the drug and to achieve ample bioavailability of the drug to induce a therapeutic effect.

11. Example VI teaches a multi-functional tablet comprising two discrete drug delivery systems i) free omeprazole and free sodium bicarbonate (rapid release) and ii) enterically coated omeprazole granules (slow release) (see [0176]; see instant claims 1-6, 10, 13, 18-21, 31). The tablet is taught to contain known binders and excipients (see [0176]; see instant claims 7 and 8). Such excipients include disintegrant such as cross-linked sodium carboxymethylcellulose (sodium croscarmellose) and fillers such as calcium lactate (see Example 1, B1 at page 10; see instant claims 8 and 28). The tablets of Example VI were formulated to deliver a bolus and a time-released dose of the PPI omeprazole (i.e. pulsed release, see instant claim 6). Upon ingestion of the tablet, the tablet dissolves, freeing the non-enteric coated base and omeprazole into the stomach (see [0176], see instant claim 22). The basic substance increases the pH of the stomach, preventing the omeprazole from acidic degradation, and allows omeprazole to be absorbed by the parental cells of the stomach. Meanwhile, the enterically coated omeprazole is absorbed in the duodenum (see [0176]; see instant claim 23, 44 and 45). It's noteworthy that four-hours post administration, the pH of the stomach is raised to an average of 7.1 (see Figure 3, see instant claim 24).

12. Although the teaching of Phillips motivates one to include an enterically coated omeprazole granule with free base and omeprazole, it still fails to teach what such an enterically coated granule is prepared from.

Art Unit: 1611

13. The teaching of Bergstrand is drawn to a pharmaceutical tablet dosage form containing omeprazole. The table of Bergstrand comprises a core substance which contains an acid susceptible substance such as omeprazole, followed by a first coating (separating layer), and then a second coating (an enteric coating) (see column 5, line 60 - column 6, line 35; see instant claims 13-17, 32+33). The separating layer includes alkaline gents to enhance the pH-buffering properties. This necessarily improves the stability of the acid labile omeprazole contained within the core as it prevents degradation of the drug during long periods of storage. Alkaline agents include compounds typically used in antacid formulations such as calcium hydroxide, sodium phosphate, and so on (see column 6, lines 20-30). The omeprazole granule of Bergstrand may be mixed with basic substances such as those discussed above (calcium hydroxide, etc.; see column 6, lines 20-30). The materials used for the enteric coating includes polyethylene glycol and polyvinyl acetate (see column 6, lines 45-55; see instant claim 27). As an example an omeprazole granule is found at Example 10.

14. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to combine the teachings of Phillips and Bergstrand because in doing so would result in a composition which possess a population comprising:

- i) a population of base (i.e. sodium bicarbonate);
- ii) a population of pharmaceutical substance (i.e. a PPI);
- iii) a population of enteric coated pharmaceutical substance; and
- iv) a population of enteric coated basic substance.

The significance of Phillips is that it teaches a multi-functional tablet compositions comprising

- i) a population of base (i.e. sodium bicarbonate);

Art Unit: 1611

ii) a population of pharmaceutical substance (i.e. a PPI);

iii) a population of enteric coated pharmaceutical substance; and

The multifunctional tablet is manufactured to possess rapid and delayed-release functionalities (pulse release) wherein the pharmaceutical substance is present in both functionalities and the basic substance is present in the rapid release portion. Although the teaching of Phillips includes an enterically coated PPI population, it fails to teach an enterically coated granule with a separating layer. One of ordinary skill would be motivated to look to the art to see how to make an enterically coated PPI granule capable of effectively delivering the active substance to the body.

15. Bergstrand teaches PPI containing granules coated with a first separating layer followed by a second enteric polymer coating, wherein the enteric granule contains antacids such as sodium bicarbonate. Thus, one of ordinary skill would be motivated to include the granule of Bergstrand with the teaching of Phillips to arrive at an invention with the instantly claimed properties (see i-iv above). With respect to the recited properties such as rapid release of the rapidly released basic substance increasing the pH of the stomach to more than 4 and less than about 7 in less than 1 hour carries no patentable weight. Such a property would be obvious to optimize, as noted above, the stability of the PPIs as well as their pharmaceutical efficacy is dependent upon the pH of their local environment. If the pH of the stomach isn't rapidly alkalinized, the drug will not be effective. Moreover, as both references are within the same general field of endeavor (delivery of antacids and PPIs), it follows that combination would be obvious and would result in a therapeutic composition having the properties of the instantly claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one ordinarily

skilled in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

19. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

Art Unit: 1611

system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/

Examiner, Art Unit 1611

January 22, 2009

/David J Blanchard/

Primary Examiner, Art Unit 1643